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REVIEW ARTICLE

A Review on Brain Cancer Mutations, Available Therapies, Existing Clinical Trials, and Forthcoming Brain Cancer Treatment

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Authors' Contributions

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ABSTRACT

Objective: This paper aims at reviewing brain cancers, types of brain cancers, and mutations.

Methodology: **M**ultiple electronic databases were searched such as Google Scholar, PubMed, HEC digital library, Elsevier, Research Gate, and Springer for all articles published in both local and international Journals for this review. Only articles written in English language were reviewed.

Mutation: The nature of the genetic mutations that induce brain cancers, as well as previously identified medicines to treat them, such as chemotherapy, steroids, and targeted therapies, have failed to explain further study and development of various drugs still in clinical trials.

Current Therapy: Temozolomide, the combined dose of Carboplatin, Melphalan, Etoposide Phosphate, Mannitol and Sodium Thiosulfate, combined therapy of Selumetinib, Dabrafenib, and Trametinib and the use of Palbociclib in chemotherapy are therapies and drugs under clinical trials aimed at replacing the traditional methods of brain cancer management therapies.

Conclusion: This review focuses on the currently available therapies for the different types of brain cancers, available clinical trial drugs for cancer, and the future of the treatment of brain cancer. Current research on brain cancer treatment is focused on delivering therapies across the blood-brain barrier to targeted mutated brain cells.

Keywords: *Brain Cancers, Brain Tumors, Glioblastoma, Prevalence, Mutations, Treatment.*

INTRODUCTION

Brain cancer may not be one of the common types of cancers affecting humans, but it is one of the most dangerous types of cancers known. Though not prevalent among global populations, it still affects a lot of people globally. Brain cancer or cancer affecting the central nervous system includes the growth of tumors at an abnormal rate inside the brain or in the spinal cord [1]. Brain tumors can be rated as primary or secondary brain tumors depending on how they occur. Advancements made in the diagnosis procedures of cancers and specifically brain cancer testing have shown the prevalence of primary cancerous brain tumors globally at an alarming rate. Most epidemiological studies do not clearly state the origin and actual causes of brain cancer and brain tumors [2].

Brain tumors are heterogeneous, meaning that they are different across patients, diagnosis, and regions based on age, gender, and genetics. The heterogeneity of the brain tumor cells has led to the existence of different types of brain cancers. Brain cancers can be described as astrocytoma, glioblastoma multiforme, and meningioma depending on how they occur and where they occur. The existence of brain cancer in heterogeneous forms has made research into the development of the brain cancer development method hard. Though there a different types of brain cancers, the Glioblastoma multiforme [GBM] has been noted by physicians and neurologists as the most common brain cancer, and that is easily managed and treated using drug treatment [3].

This paper presents an overview of brain cancer. It will discuss the types of brain cancers, present summarized statistics of brain cancer risks, prevalence, deaths, and survival rates, present the causes of brain cancers will also discuss brain cell mutations and the causes of the mutations. It will make a presentation of the currently available treatment options for brain cancer, the challenge of the blood-brain barrier in administering brain cancer therapeutics, and finally the future of the treatment of brain cancer. A brain tumor can be seen in Figure **1**.

BRAIN CANCER RISKS, PREVALENCE, DEATHS, AND SURVIVAL RATES

A histology study of malignant brain and other central nervous system tumors as presented by Leece *et al.,* 2017 [4], based on data drawn from the Central Brain Tumor Registry of the United States [CBTRUS] and the International Agency for Research on Cancer's [IARC] carried out in 2003–2007 notes that.

"There were significant differences in incidence by region. Overall incidence of malignant brain tumors per 100000 person-years in the US was 5.74 [95% CI = 5.71–5.78]. Incidence was lowest in Southeast Asia [AAIR = 2.55, 95% CI = 2.44–2.66], India [AAIR = 2.85, 95% CI = 2.78–2.93], and East Asia [AAIR = 3.07, 95% CI = 3.02–3.12]. Incidence was highest in Northern Europe [AAIR = 6.59, 95% CI = 6.52–6.66] and Canada [AAIR = 6.53, 95% CI = 6.41–6.66]. Astrocytic tumors showed the broadest variation in incidence regionally across the globe."

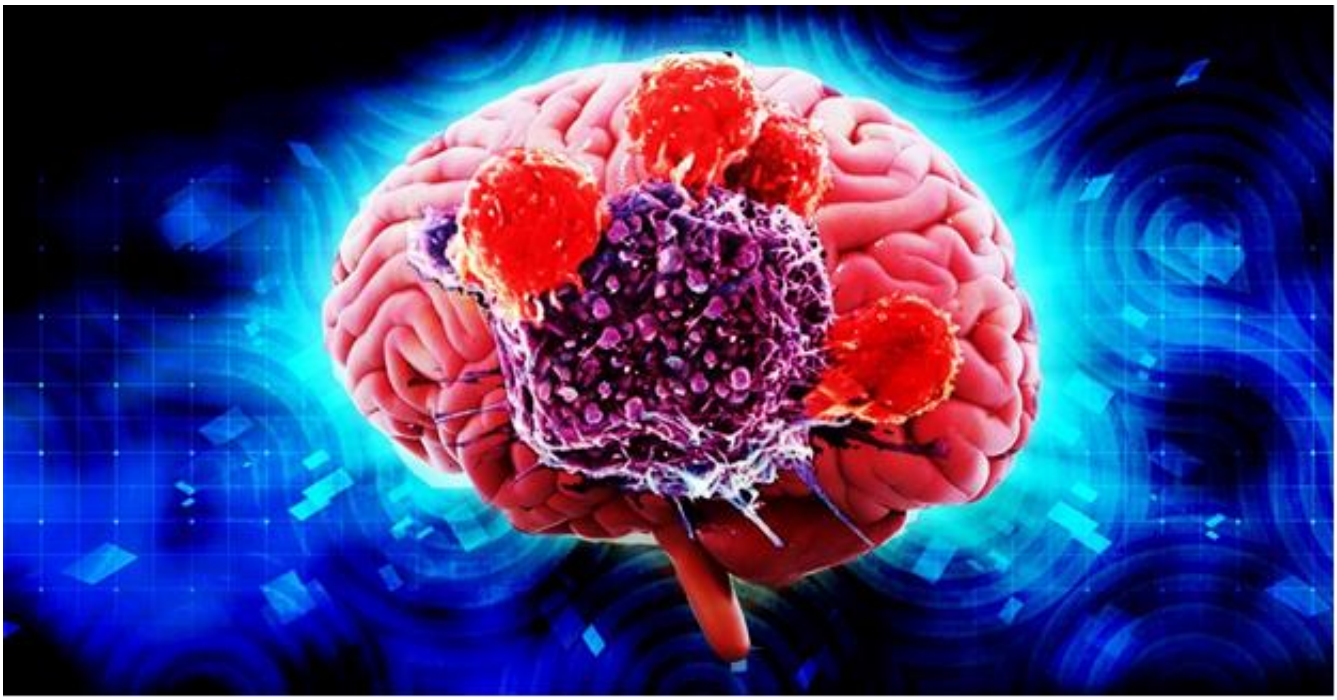

Figure 1. A Brain Tumor, Source.

Brain tumor statistics published on the cancer information website [5], notes that in 2020 alone, the risk of cancer diagnosis in the United States stands at an estimated 13,5890 and 10, 300 new male and female cases of cancerous tumors of the brain and spinal cord respectively. These statistics are only for the primary tumors that affect the central nervous system persons as the probability of developing brain metastases in a lifetime is low and remains at under 1% of a new brain cancer diagnosis with the primary brain tumor diagnosis accounting for an estimated 90% of the brain cancer prevalence and risks.

Onhealth.com, 2020 [6], reports that:

"*Approximately 200,000 to 300,000 people per year in the U.S. suffer from tumors that start elsewhere in the body and then spread, or metastasize, to the brain. Approximately 50% of cancers found in the brain begin as lung cancer that later spreads to other organs including the brain. Other cancers that may spread to the brain include those of the colon, breast, kidney, and melanoma, a potentially deadly type of skin cancer. At least 80% of tumors in the brain occur as multiple growths in the brain. Another 10% to 20% of tumors that have metastasized to the brain are single tumors."*

Surveillance reports on brain cancer and its mortality and morbidity rates produced by the Surveillance, Epidemiology, and End Results [SEER] [7], shows that the number of brain cancer and other nervous system cancer cases between the year 2012 and 2016 stood at 6.4 per 100,000 for both male and female cases per year and the deaths from brain cancer and associated nervous system cancer were at 4.4 per 100,000 of the male and female populations a year. Another report drawn from the National Brain Tumor Society of brain cancer and brain tumors measured between 2010 to 2014 shows that the rate for malignant and non-malignant brain tumors and those affecting the central nervous systems was at 22.64 per 100,000 people out of the 379,848 cases during the 5-year observation.

The SEER cancer report further adds that based on the data collected between the same period [2014-2016] on the people at risk of developing cancer and the prevalence of cancer showed that an estimated 0.6 percent of the population in the US were at risk of getting diagnosed with brain cancer, brain tumors and other cancers that affect the nervous system [7]. An estimated 78,980 new cancerous brain tumor cases were reported in the United States alone creating a picture of the global cancer cases.

Statistics on cancer incidences, mortality, and survival rates adapted from the American Cancer Society's publication, Cancer Facts & Figures 2020, the ACS, the CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016, and the National Cancer Institute websites in January 2020 and presented by "Cancer.net, 2019" [8], to explain the survival rates based on a 5-year observation of survival rates of brain cancer show that:

"The 5-year survival rate for people with a cancerous brain or CNS tumor is almost 36%. The 10-year survival rate is almost 31%. Survival rates decrease with age. The 5-year survival rate for people younger than age 15 is more than 74%. For people aged 15 to 39, the 5-year survival rate is about 71%. The 5-year survival rate for people aged 40 and over is about 21%. However, survival rates vary widely and depend on several factors, including the type of brain or spinal cord tumor. Talk with your doctor about what to expect with your diagnosis."

SEER on the prevalence report showed that an estimated 165, 813 people in the United States were living either with brain cancer or cancer that affected their nervous system. An estimated 3,540 children under the age of 15 are also at risk of been diagnosed with a brain or CNS tumor in 2020 and a further estimated 10,190 and 7,830 deaths of male and female cases previously diagnosed with a cancerous brain tumor are predicted to occur despite the existing control and treatment therapies [7]. Brain cancer has been associated with an estimated 10,000 annual deaths of children below the age of 15 years and with over 20, 000 diagnosed cases annually [9].

BRAIN CANCER AND GENE MUTATIONS

The deadly brain cancer is a result of genetic mutations [10]. Previously, the mutations leading to the development of brain cancer were not identified. The advancements made in cancer diagnosis technologies have been able to uncover the genes responsible for the mutations leading to the development of the most and aggressive types of brain cancers. The identifications of the mutant genes were made on the genetic genes responsible for Glioblastoma multiforme and Glioma. Most of these

mutations have been identified to be hereditary in mutation carrier genes [11]. Some genetic mutations are responsible for the development of Glioblastoma multiforme as discussed by [12], based on reviewed studies on glioblastoma and genetic mutations noting that:

"Form and analysis of more than 1,500 genetic combinations in mice, researchers identified some genes, including B2m-Nf1, MII3-Nf1, and Zc3hf3-Rb1, that work together to cause glioblastoma."

Richards *et al* [10], describe the genetic mutations in the identified gene IDH1 to be associated with most of the aggressive brain cancers. Most of the mutations leading to grade II and III gliomas are a result of the mutations in the IDH1 gene [13]. These mutations have been associated with the resistance of aggressive brain cancers to treatment therapies such as chemotherapy [14a].

TYPES OF BRAIN CANCER

Hundreds of brain tumors may be cancerous or non-cancerous [4]. Brain cancers can be divided into Astrocytoma, Meningiomas, and Glioblastoma multiforme.

Astrocytoma

Astrocytoma, according to the American Cancer Center [4]. develops from anywhere in the central nervous systems mostly in the cerebrum and in the spinal cord. As this part of the brain is responsible for several body functions, astrocytoma has been associated with changes in behavior and seizures. These are the most common types of brain tumors affecting most of the Astrocytoma are linked to most of the serious central nervous systems gliomas and other conditions [15]. Astrocytoma may be of any grade of brain cancer. An example of an astrocytoma is the aggressive glioblastoma multiforme.

Meningiomas

Meningiomas form most of the common brain tumors that affect the meninges [16]. Meningiomas mimic other tumors posing a threat to misdiagnosis [17]. Meningiomas affect the cell membrane of the brain and the spinal cord [4].

Glioblastoma multiforme [GBM]

Glioblastoma multiforme is an aggressive and most common type of astrocytoma that affects different parts of the brain and most common in elderly patients [18]. Though the glioblastoma multiforme type of brain cancer is aggressive and infiltrative, its occurrence outside of the brain is rare. The development of this type of skin cancer seems to develop from lower grade [I & II] to more dangerous grade IV tumors [19]. Glioblastoma multiforme is associated with low survival rates and a lack of high response treatments [20]. This means this type of brain cancer has a high mortality rate and mostly due to its aggressiveness leads to treatment failure. Symptoms, Treatment, and Prevalence of glioblastoma can be seen in Figure **2**.

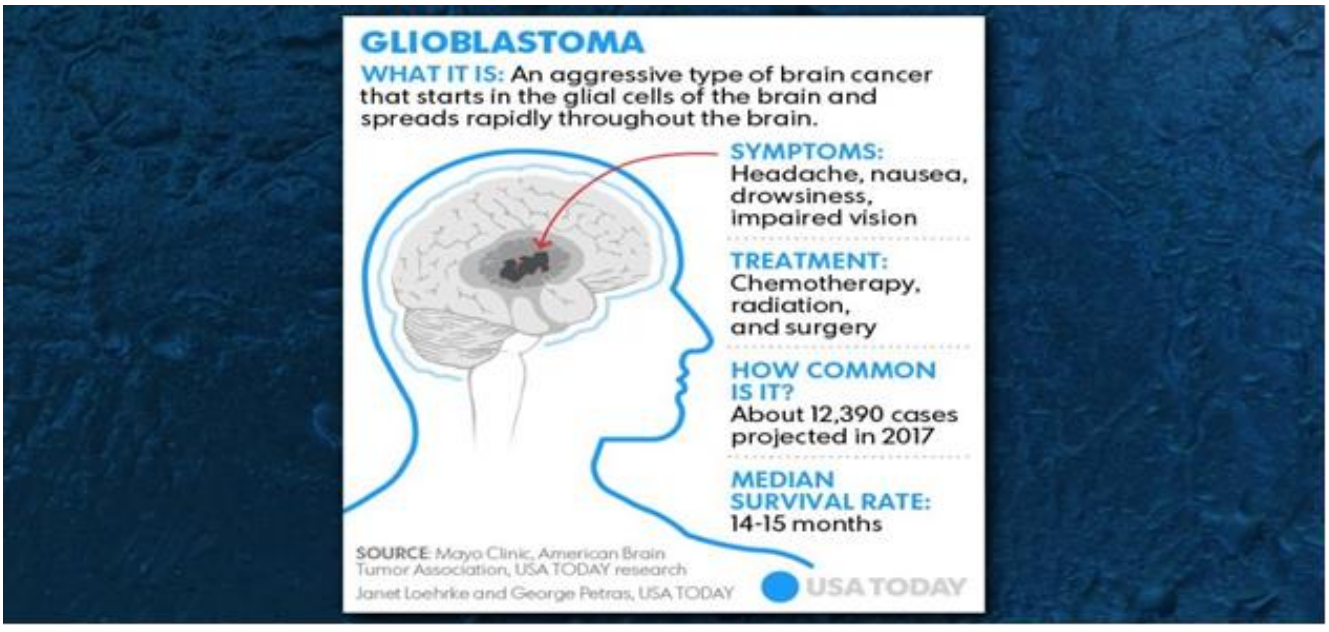

Figure 2. Glioblastoma: Symptoms, Treatment and Prevalence, Source.

Craniophargnyoma

Craniophargnyomas are a rare type of epithelial tumors mostly affecting children and older adults, but can also get diagnosed at any age [21]. Craniophargnyomas have been found to develop near the pituitary gland posing a threat to certain body functions such as vision, the production of essential hormones such as those responsible for growth [22]. Complete removal of the craniophargnyomas is very difficult owing to the location of these tumors in brain which may lead to reoccurrences of the tumors requiring multiple reoperations [23].

CURRENT TREATMENT OF BRAIN CANCER

Cancer has been noted to have many side effects such as fatigue and inflammation due to cancer before and even after treatment making it crucial to consider its treatment and the type of treatment chosen [24]. The treatment of brain cancer and brain tumors has been elusive for so long despite the numerous medical studies due to the complex molecular pathology and biology of brain cancer which makes it advanced and results in the earlier discussed numerous mutations [25]. Though a lot of research has been directed to the understanding of brain cancer and brain tumors, brain cancer and cancers at large remain to be one of the deadliest forms of cancer today. The elusiveness of brain cancer cells from all conventional approaches to cancer treatment is associated with cancer cells' unique biology and the extracellular environment of the neural cells [26]. However, some advancements have been achieved that is aimed at if not eliminating brain cancer and brain tumors, to be able to control the development of the cancer cells. The treatment for brain cancer is dependent on some factors. The type of treatment chosen for the brain cancer and brain tumor is dependent on the size, type of the tumor, and the location of the tumor.

Chemotherapy

Chemotherapy has been the most preferred method of brain cancer therapy, but it is growing ineffective due to many reasons. The treatment of malignant brain tumors poses a lot of challenges due to the heterogeneity of the cancer cells making it hard to diagnose, treat and manage [27]. Due to this and the aggressive nature of the chemotherapy process and the impact, it has on the central nervous system, the method of brain cancer treatment has grown ineffective pushing medical researchers to focus on new and improved methods of brain cancer management.

Steroids

Steroids such as glucocorticoids have been applied in the clinical treatment of brain tumors [28]. These steroids assist the patients to control the side effects of undergoing radiotherapy. Other steroids such as corticosteroids though they have been observed to harm the survival chances of a brainer cancer patient undergoing therapy, they have been applied in the testing of the patient's response to other type brain cancer treatment therapies such as chemotherapy [29].

Targeted therapy

Targeted drug delivery seeks to bypass the blood-brain barrier [30]. The targeted drug delivery has revolutionized the way brain cancer therapies are carried out and paved the way for the development of other related and advanced drug delivery systems [31]. The targeted drug delivery application as an anticancer procedure in the treatment of brain cancer has made it easy to get brain cancer therapeutic drugs across the blood-brain barrier and improving the drug uptake during brain cancer therapies [32]. Targeted therapy is now becoming the basis for most of the currently developing brain cancer treatment methods to be used in the future for cancer treatment.

CLINICAL TRIAL DRUGS FOR THE TREATMENT OF BRAIN CANCER

A lot of progress has been made in the development of therapeutics for different purposes in the treatment of brain cancer. Some drugs and therapies have been developed to cure some types of cancer while others have been developed to control the development of brain tumors and the control the metastatic spread of primary cancer cells to other organs such as the brain from other affected body parts. The much progress made in the development of trial drugs for the treatment of cancer includes the molecular target agents and other novel immunotherapies which have been modified to achieve efficiency in the control or elimination of primary tumors before they spread [33]. The development and applications of

immunotherapies as an approach to the management and treatment of brain cancer are further discussed under the topic of future treatment of brain cancer. Different clinical trial drugs have been developed for different types of drugs. A number of these trial drugs for human brain cancer patients include:

Low dose whole-brain Radiation therapy with Temozolomide

Temozolomide is used in clinical trials for the treatment of newly diagnosed Glioblastoma Multiforme, central nervous systems lymphoma, and other brain metastases concurrently with whole-brain radiation therapy [34]. Temozolomide is used in clinical trials with high-energy radiation therapy. The use of Temozolomide concurrently with the high-energy x-rays has been displayed to produce a high potential response rate in the shrinking of brain metastases and the treatment of metastatic melanoma [34,35].

A combined dose of Carboplatin, Melphalan, Etoposide Phosphate, Mannitol, and Sodium Thiosulfate

These drugs are clinically tested together as a combined dose during chemotherapy for the cure of recurrent brain tumors. Mannitol is applied in the attempts of improving the blood-brain barrier permeability [36,37]. Mannitol is used to improve drug delivery during clinical trials for chemotherapy drugs such as Carboplatin, Melphalan, Etoposide Phosphate, and Sodium Thiosulfate [38].

Selumetinib

Selumetinib is used in clinical trials of retreatment of refractory Glioma [39]. The drug has also shown effectiveness as a mediator in trials for the treatment of medulloblastoma [40]. Selumetinib is also in a trial to be used as a MEK inhibitor in the treatment of patients with recurrent glioma [41].

Dabrafenib and Trametinib combined therapy

The combined Dabrafenib and Trametinib therapy are under investigation to be used as an inhibitor for mutant metastatic melanoma [42]. The continued trials and improvements have shown the combined therapy can be targeted as an inhibitor has shown increased efficiency and effectiveness in the treatment of advanced cases of untreated mutant metastatic melanoma [43].

Palbociclib in Chemotherapy

Palbociclib is used as a combination drug during chemotherapy as a treatment for glioblastoma as an inhibitor for cyclin-dependent kinase [44]. Palbociclib is also used in clinical trials for the treatment of brain metastases using chemotherapy [45].

BLOOD-BRAIN BARRIER AND BRAIN CANCER TREATMENT

The pharmaceutical industry has experienced a lot of advancements in Neurotherapeutics which have given hope to cancer patients and cancer researchers. Some drugs and therapies have been developed with the potential to cure or control the development of brain cancer cells however such developments have been limited due to the issues associated with the blood-brain barrier [BBB] [46]. The blood-brain barrier "is a continuous endothelial membrane within brain micro-vessels that has sealed cell-to-cell contacts and is sheathed by mural vascular cells and perivascular astrocyte end-feet." [47]. The BBB is made of specific physical and enzymatic components and transports responsible for the maintenance of a desired extracellular environment for the normal functioning of the central nervous system [CNS] [48]. Apart from the blood-brain barrier playing the key function of ensuring a specialized extracellular environment for the central nervous system; it is also responsible for the maintenance of systematic compartment communication [49].

The BBB maintains a complex and extracellular environment for the integrity of the brain and within the central nervous system [50]. The blood-brain barrier can simply be described as a protector for the complicated neural network system from the pathogens that may attack the body, changes in the body's metabolism, and from other molecules that may exist in the body and the blood but that harm the brain. The blood-brain barrier creates a protective essential clear boundary separating the central nervous systems and related neural system from the blood in circulation and protects the brain from infections by regulating brain processes and the movements of ions and molecules from the circulating blood into the CNS [51]. This means that that the BBB is extremely selective when it comes to what molecules enter from the blood vessels into the central nervous system. This dedicated control of

brain hemostasis by the blood-brain barrier has become a problem when it comes to the control and treatment of brain pathologies.

The efficiency in the permeability of the blood-brain barrier by different substances and molecules is crucial to the overall health of the brain and in the healing of all brain diseases such as the numerous forms of brain cancer. Almost all the drugs developed for the treatment of brain pathologies including brain cancer are mostly large molecule drugs [52]. Though the development of the drugs for the treatment and control of the brain has advanced and achieved great milestones, the greatest problem and barrier to the treatment of brain cancer remains in the target delivery of the developed brain cancer pharmaceutical drugs to the brain across the blood-brain barrier [53]. These current brain cancer treatments and therapies are facing the greatest challenge due to the controlled brain hemostasis and insufficiency of available drugs to penetrate the blood-brain barrier [54]. The BBB has made it hard to systematically delivered drugs to penetrate the brain making it the greatest barrier today to successful and effective brain cancer treatment [55]. The future of brain cancer treatment needs to and is focused on developing methods that improve the permeability of the blood-brain barrier by the systematically administered cancer therapeutics.

THE FUTURE OF BRAIN CANCER TREATMENT

Despite all the research and investments made at finding appropriate treatment and cure for brain cancer, it remains the deadliest of all types of cancer. In modern times and with the advancement of technologies that support research, the future of treating deadly brain cancer looks promising. Research on findings methods of treating brain cancer has been focused on finding ways of bypassing the blood-brain barrier. Based on past statistics on the use of current brain cancer treatment approaches such as invasive surgical resection, chemical and radiotherapy have shown to result in numerous deaths and unsuccessful elimination of the malignant brain tumor cells due to the aggressive nature of the approaches and the complexity of the brain [56]. To deal with such, researchers have kept on finding new approaches and methods to the treatment of brain cancer that have a little invasion of the brain and with less mortality rates. Some of the approaches to modern and future treatment of brain cancer include immunotherapy, laser thermal ablation, implantable ultrasound, and Aryl Hydrocarbon Receptor specifically applied in the control and treatment of Glioblastoma multiforme [GBM]. Some of these techniques and approaches are in partial use while others are still in testing and development phases.

Immunotherapy

The existing drugs used in the treatment of brain cancer and offering support to brain cancer patients are growing ineffective to the heterogeneous brain cells. Medical researchers on the disease have started to reanalyze the disease to develop new drugs to treat and control the development of malignant brain tumors. Different feasibility tests have been carried out to test the feasibility of immunotherapy. Jackson *et al* [14b], describe immunotherapy as:

"*An emerging as the newest pillar of cancer treatment, with the potential to assume a place alongside surgical debulking, radiotherapy, and chemotherapy."*

The development of immunotherapy is in line with the developments made in imaging technologies to achieve improved cellular therapy in the treatment of malignant brain tumors [57]. Immunotherapy in the treatment of cancer involves the introduction of modified viruses into the body to stimulate an immune response that attacks malignant brain tumors [58]. The immunotherapy approach has been referred to as the future of not only the treatment of brain cancer but also in other medical applications to treat other diseases.

Laser thermal Ablation

As the currently existing methods of brain cancer treatment are proving to be infective against the continuously developing brain cancer, different approaches to the treatment and control of malignant brain tumors are being developed. The recently developed and under test for wider clinical application is the use of laser thermal ablation neurosurgical technique. Various studies and medical research have been conducted to test the effectiveness of the use of the laser ablation neurosurgical technique. Tests on the use of particle-assisted laser ablation in the treatment of brain tumors using canine brain models and noted that the use of the particle-assisted

laser ablation was successful and effectively and selectively treated the intracranial tumor [59] [Schwartz *et al.,* 2009]. Tests carried out in the testing of the use of MRI-guided laser thermal ablation in epilepsy surgeries have proved that it is possible to carry out less invasive surgeries successfully. A test on the use of hyperthermic laser ablation on recurrent gleesome showed that it induced temporary hyperthermia allowing the delivery of brain cancer therapeutic drugs across the blood-brain barrier [60]. These successful test applications of the use of the laser thermal ablation surgery techniques create new approaches to the removal of solid malignant brain tumors in the future. The use of laser thermal ablation neurosurgical technique is promising to be disruptive in how brain surgeries are carried and having a crucial application in brain cancer application can be seen in the given Figure **3**.

Implantable Ultrasound

After years of trials and errors, the use of chemotherapy brain cancer treatment and control has proved to be an ineffective approach to the treatment of brain cancer. This has much been associated with the challenges posed by the blood-brain barrier to the penetration of the schematically administered brain cancer-treating drugs [51]. Apart from the use of chemotherapy, surgery has been the only sure way of delivering drugs to the malignant brain tumor cells or to remove the solid tumor [52]. Based on the various past research aimed to aim at opening the blood-brain barrier to deliver brain cancer pharmaceutical drugs to the developing malignant brain cancer tumors, it has been proven that the use of a high-density targeted ultrasound can open the blood-brain barrier and deliver brain cancer-curing drugs [61]. With the technological advancements made in the modern world and the medical sector, the use of high-density ultrasound combined with the improved medical imaging technologies making it easy to open the BBB to deliver cancer drugs to targeted brain cancer cells and at the same time avoiding the invasive surgeries [52]. Due to the limitations to drug delivery to the brain posed by the blood-brain barrier tried an approach of using ultrasound combined with microbubbles to increase the permeability of blood vessels by brain cancer drugs thereby, the use of high-density ultrasound allowed the drugs to permeate the blood vessels into the targeted brain cancer tumors [62]. These advancements in ultrasound technologies combined with microbubbles to assist in the permeability of the blood-brain barrier during drug delivery in curing brain cancer can be further developed to become the future of therapy in brain cancer treatment is shown in the Figure **4** [63].

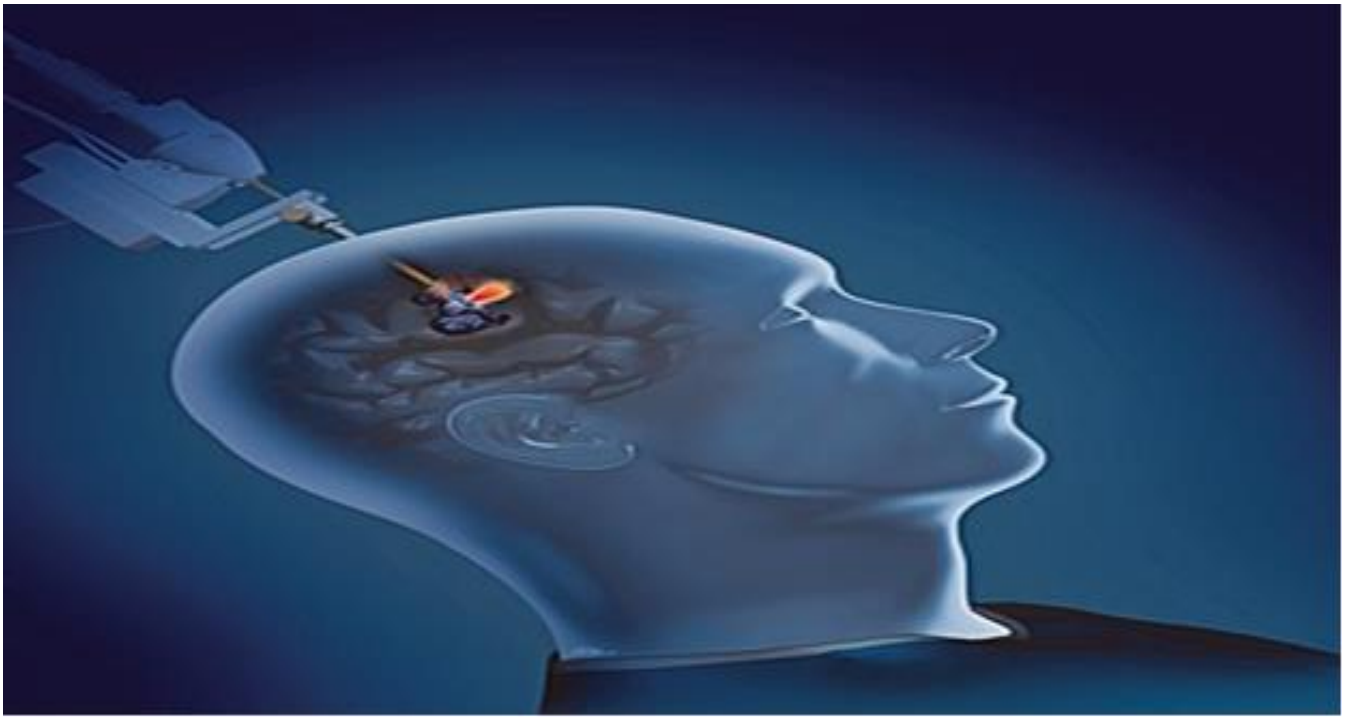

Figure 3. Laser Thermal Ablation Brain Cancer Treatment, Source.

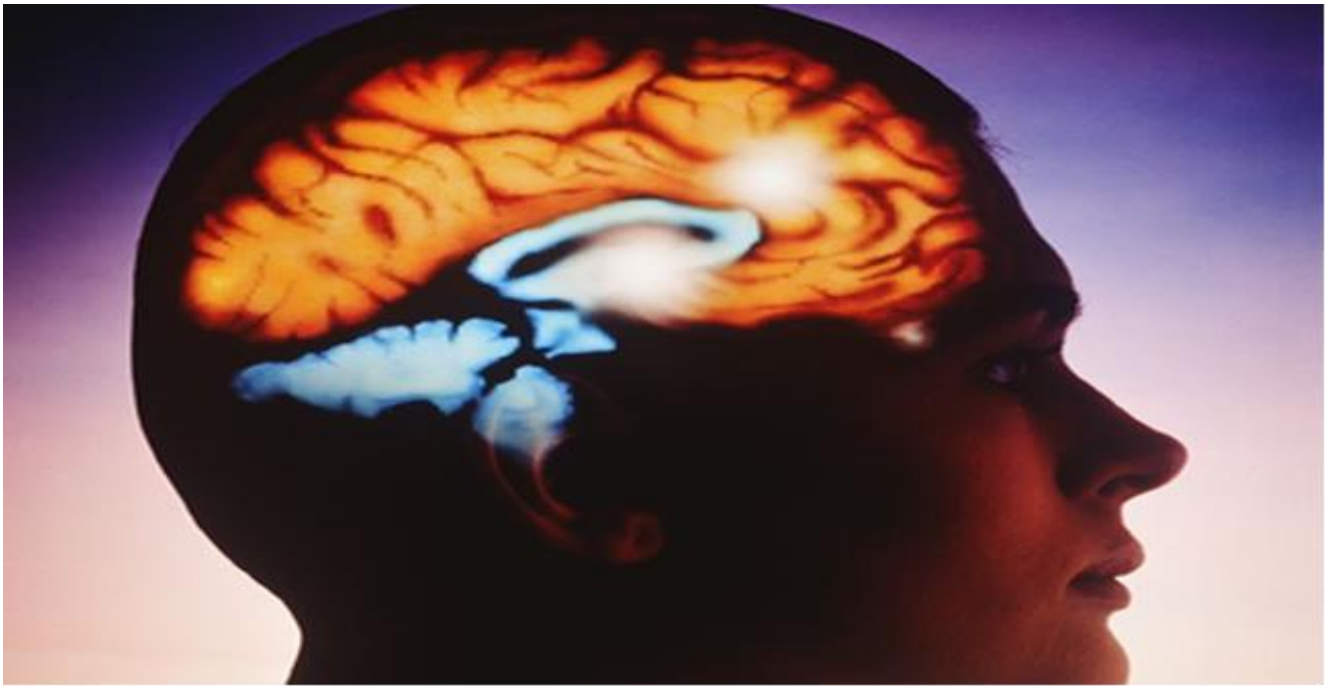

Figure 4. Implantable Ultrasound, Source.

The use of Aryl Hydrocarbon Receptor in Control and Treatment of Glioblastoma Multiforme [GBM]

The Glioblastoma multiforme [GBM] is the most common malignant brain tumor [3]. Previous drug trials have been successful in the control and cure of the glioblastoma multiforme but serious side effects to the patients. Continued research has ventured into a safer and sure method of curing the GBM. The use of the Aryl hydrocarbon receptor has been tested and proven to work when used as a cure for the glioblastoma multiforme. The Aryl hydrocarbon receptor [AhR] has been tested in improving the permeability of the blood-brain barrier due to its function in the maintenance of cellular homeostasis and its role in pathophysiology [64]. The working process of the Aryl hydrocarbon receptor is activated by xenobiotic toxins in its environment [65]. As the human AhR must be activated by environmental toxins, its activation in physiological conditions is still not sufficiently researched. Clinical studies and tests have been carried out in mice in which the human Aryl hydrocarbon receptor was noted to work as a tumor suppressor-like gene in cases where glioblastoma multiforme was targeted [64]. The activation of the human AhR is a physiological condition in the absence of environmental toxins based on some studies that have shown to be due to the production of sufficient amounts of kynurenine during the development of cancer cells and the resulting inflammation of the extracellular neural environment [65-66]. There is a need for further investigation and the development of the Aryl hydrocarbon Receptor due to its potential to be used in the targeted treatment of Glioblastoma multiforme in patients who have the Aryl hydrocarbon receptor [64].

CONCLUSION

Cancer has become one of the most dangerous diseases today. It is rated as the world's 10th cause of human deaths in modern times. A lot of research is focused on developing new approaches to the treatment of brain cancer as current methods of treatment prove to be ineffective. Some factors are based on the privileged nature of the brain such as the extracellular environment that creates a blood-brain barrier reducing the permeability of the neural blood cells. The limitations of the use of humans to test and develop cancer drugs and therapies have limited the developments that be made in the development of drugs that completely cure brain cancer. Cancer, based on global statistics on risk, prevalence, death, and survival, can be rated as one of the top ten causes of death for both adult male and female patients. With the advancement of research on brain tumor cells and the more refined nature of cancer cells, the future of treatment of brain cancer looks promising giving hope to many already suffering

brain cancer patients. Medical research and technological developments made in the field of medicine and directed towards the treatment of brain cancer have made it possible to develop future cancer treatment approaches such as immunotherapy, laser thermal ablation, implantable ultrasound, and Aryl Hydrocarbon Receptor specifically applied in the control and treatment of Glioblastoma multiforme [GBM] which are opening new windows and hope to eventual containment and absolute curing of brain cancer.

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